
Memorial Sloan Kettering
Cancer Center

# Acoustic Imaging

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# Common aspects of all imaging

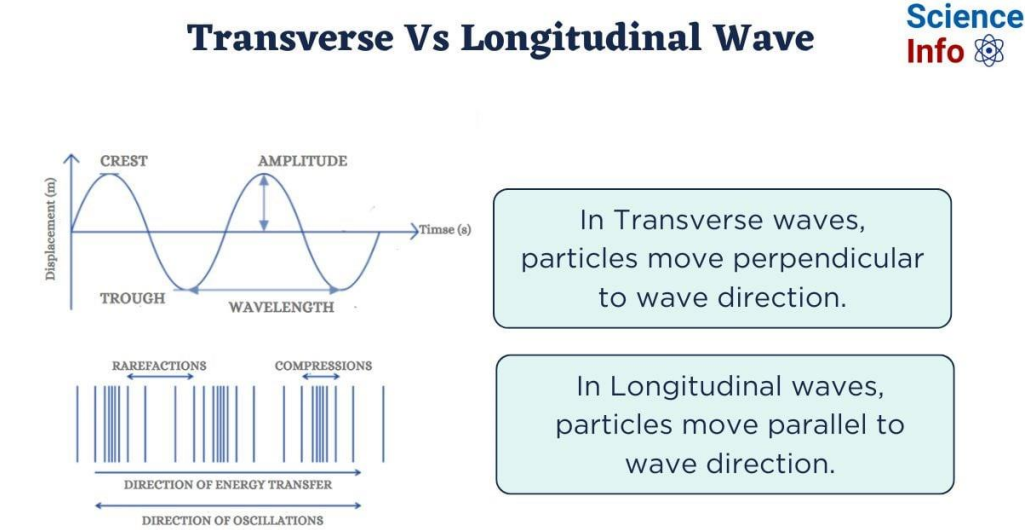
1. Source of signal
   - Light, sound, radioactive decay, magnetic moment etc.

2. Method of detection
   - How does the signal get captured?
   - How is the signal processed/converted into interpretable data

3. Generation of images
   - What creates contrast?
   - SNR and not signal is what matters
   - Does contrast represent a qualitative or quantitative metric?
   - Is the contrast coming from a material property or a biological function?

# In acoustics the source of signal is sound

- Sound is also a particular form of energy
- Sound: a vibrations that propagates through a medium


A few important parameters for us:

- Amplitude
- Wavelength / Frequency
- Direction of propagation
- Phase
- Speed

A few differences with light

- Longitudinal wave
- Requires a medium
- No polarization

# Fundamentals of sound

- Our ears translate patterns of vibrations into "meaning"
- A few basic equations

$$v = \lambda f$$

$$\text{light: } v = \frac{c}{n} \qquad \text{sound: } v = \sqrt{\frac{B}{\rho}}$$

$B$ is the bulk modulus of the medium
$\rho$ is the density of the medium

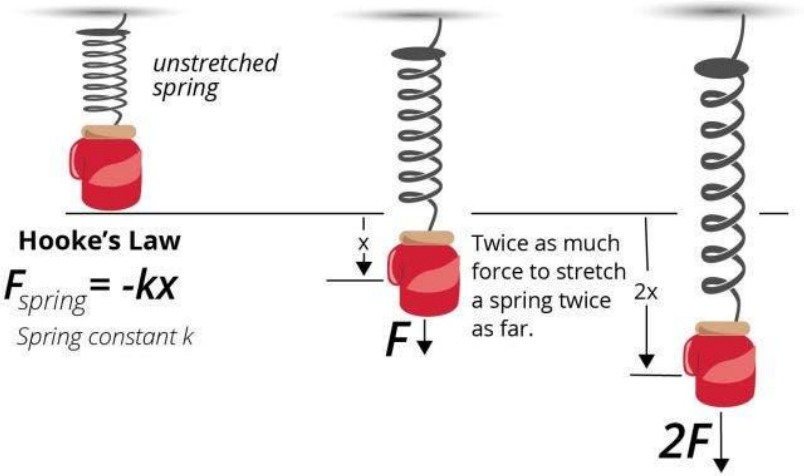
- Bulk modulus is a measure of material stiffness (resistance to compression)
- Another useful metric of sound resistance is acoustic impedance: $Z = \rho v$
- Units of speed, frequency and wavelength are the same: m/s, Hz, m
- Units of density, $\rho$, are kg/m$^3$
- Units of bulk modulus, B, are Pascals [Pa]
- Units of impedance, Z, are Rayls = kg/m$^2$s

# A bit of background on material stiffness

Hooke's Law: $F = -k\,x$

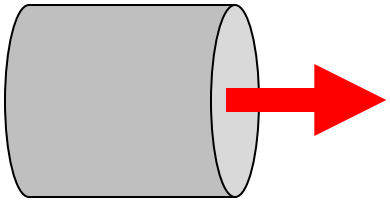
k is the spring constant [N/m]

Does the stiffness of the spring depend on its length?



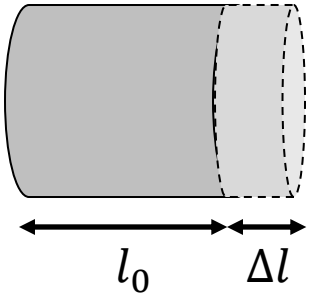

- Spring constant is not a material property
- Limited utility in describing biological material
- Many applications and large modeling potential in biology
  - Modeling DNA coiling / uncoiling
  - Tension sensors
  - Optical tweezers
  - Many others

# A bit of background on material stiffness



Apply a stress, σ

$$\sigma = \frac{Force}{area}$$




Results in a strain, $\varepsilon$

$$\varepsilon = \frac{\Delta l}{l_0}$$

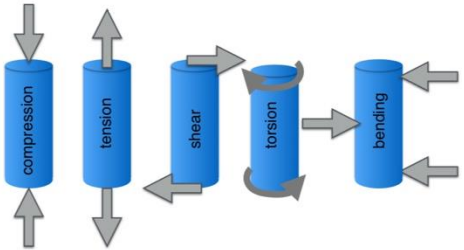
Units of stress are $N/m^2$ = Pa

Units of strain are none

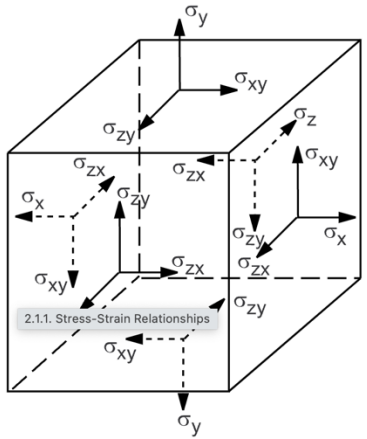
How are stress and strain related? $\sigma = E\,\varepsilon$

E is called Young's modulus and its units are Pa

- Young's modulus is a material property




- In reality, E is a matrix with components $E_{xx}$, $E_{xy}$, $E_{xz}$ etc

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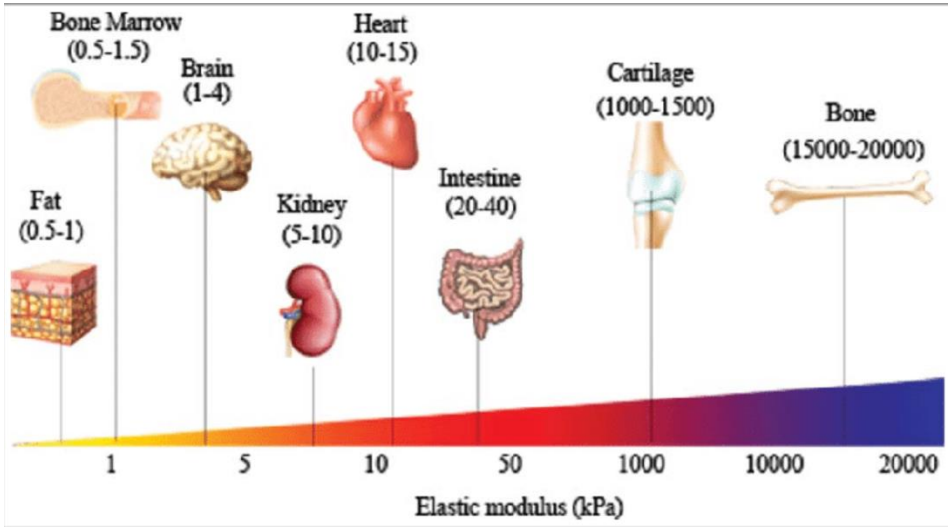
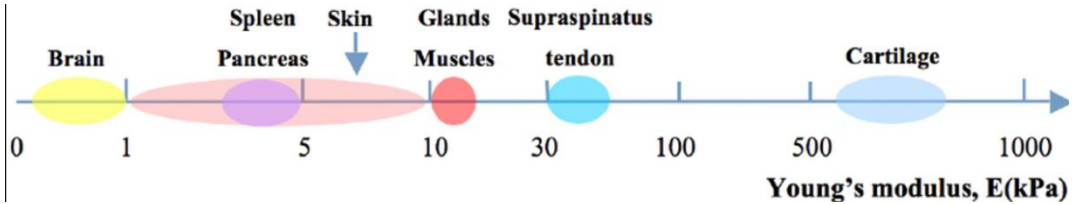
# Young modulus of common biomaterials




Handorf, Andrew & Zhou, Yaxian & Halanski, Matthew & Li, Wan-Ju. (2015). Tissue Stiffness Dictates Development, Homeostasis, and Disease Progression. Organogenesis. 11. 1-15. 10.1080/15476278.2015.1019687.




Liu, Juan & Zheng, Huaiyuan & Poh, Patrina & Machens, Hans-Günther & Schilling, Arndt. (2015). Hydrogels for Engineering of Perfusable Vascular Networks. International Journal of Molecular Sciences. 16. 15997-16016. 10.3390/ijms160715997

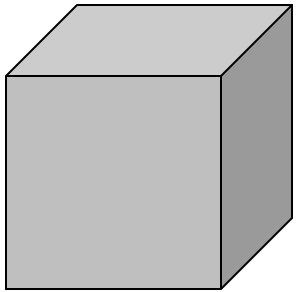
| Material | Young's modulus |
|---|---|
| Diamond | 1220 GPa |
| Steel | 200 GPa |
| Tooth enamel | 20–84 GPa |
| Wood (oak) | 11 GPa |
| Vulcanized rubber (e.g. car tyres) | 0.01–0.1 GPa |
| Silicone rubber (e.g. wristband) | 500–5000 kPa |
| Tendon | 800 kPa |
| Cancerous soft tissues | 20–560 kPa |
| Healthy soft tissues | 0.5–70 kPa |

Hoskins, Peter. (2012). Principles of US elastography. Ultrasound. Ultrasound. 20. 8-15. 10.1258/ult.2011.011005

- Useful to have a sense of stiffness of different materials
- Both from detection perspective and from engineering perspective of making biomimetic and other materials

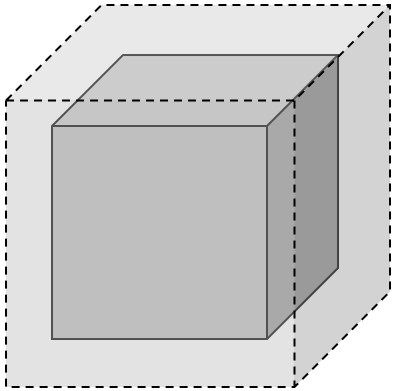
# What is bulk modulus?

Bulk modulus, B, is analogous to Young's modulus but in 3D



Apply pressure: -ΔP

$V_0 \rightarrow V_0 + \Delta V$



$$\varepsilon = \frac{\Delta V}{V_0}$$

$$\Delta P = -\varepsilon \, \mathrm{B}$$

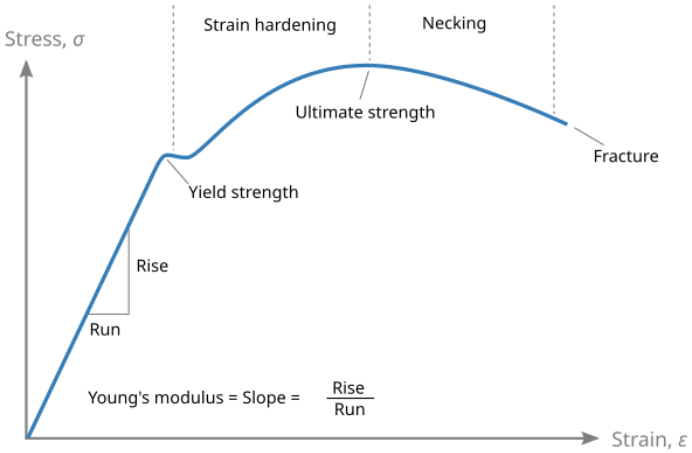
Units of bulk modulus are Pa

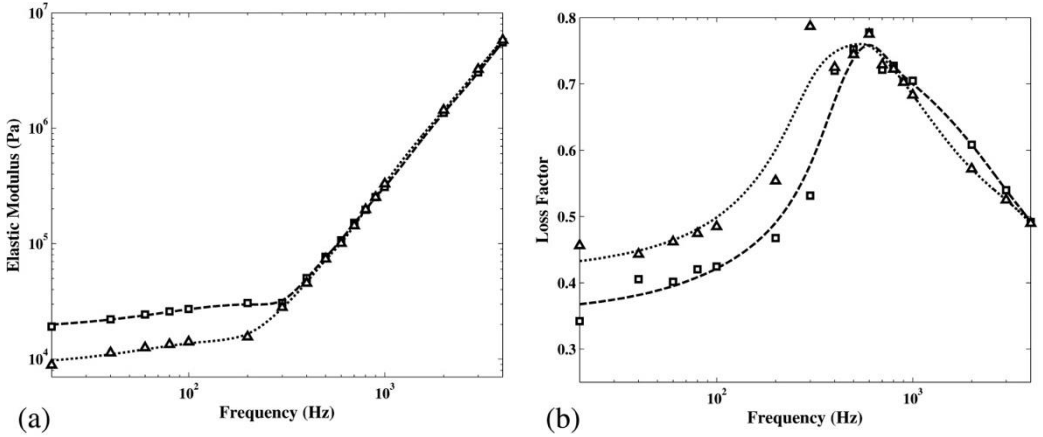
Like Young's modulus, bulk modulus is a material property

Given that sound travels through materials through vibrations (i.e. deformation of the material), this property is an essential part of acoustics.

# Elastic and bulk modulus dependence

## Viscoelastic materials




Kazemirad S, Heris HK, Mongeau L. Experimental methods for the characterization of the frequency-dependent viscoelastic properties of soft materials. J Acoust Soc Am. 2013 May;133(5):3186-97. doi: 10.1121/1.4798668.

## Viscous materials

- Essentially no storage modulus, but have viscosity
- Bulk modulus has little dependence on frequency

# Intensity of sound

$$I = \frac{(\Delta P)^2}{2\,\rho\,v}$$

$\Delta P$ is the pressure variation
$\rho$ is the density of the medium
$v$ is the speed of sound in the media

Does the bulk modulus not matter?

$$v_{sound} = \sqrt{\frac{B}{\rho}}$$

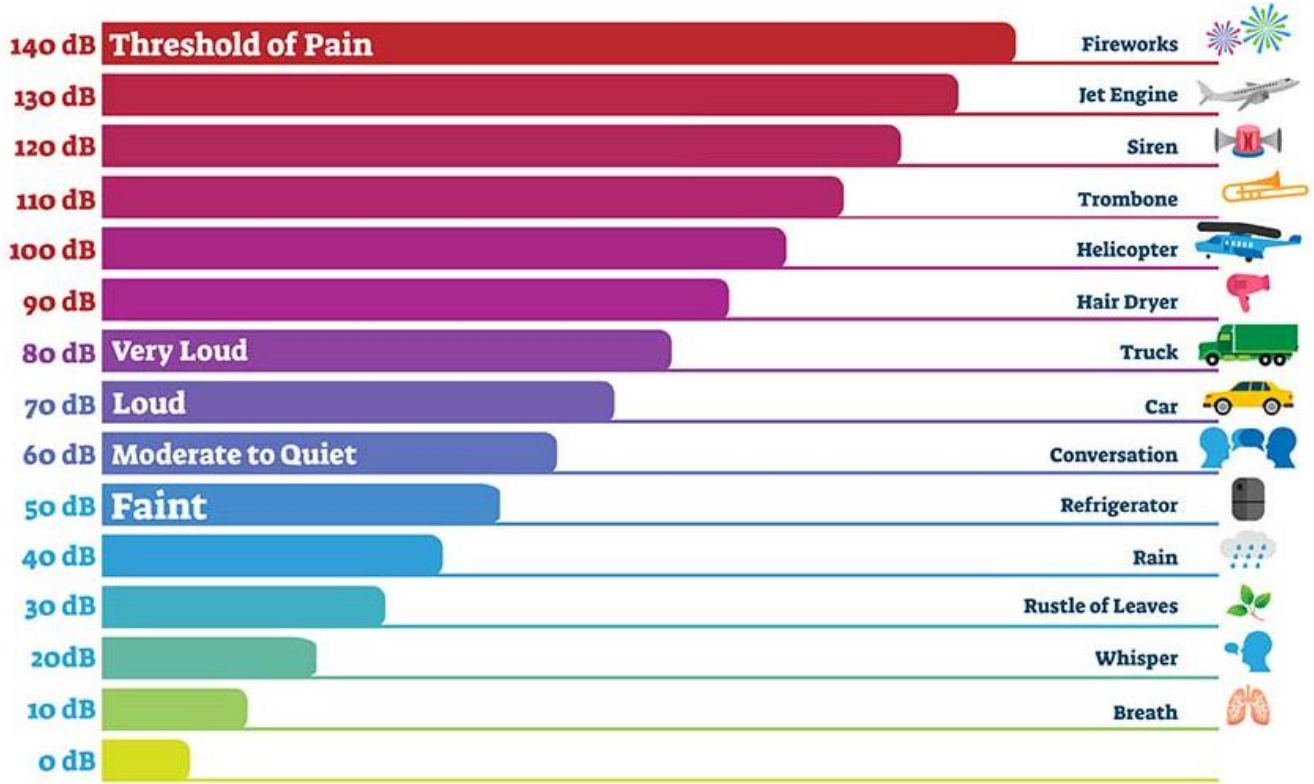
$Z = \rho\,v$ Acoustic impedance [Rayl = kg/m²s]

Intensity is measured in *W/m²*

$$\beta = 10\ log_{10}(\frac{I}{I_0})$$

This is another measure of sound intensity in decibels (dB)
$I_o$ is a reference intensity of $10^{-12}$ W/m²

# Intensity of sound




Typical sonograms are in this range.

How come we can't hear a sonogram?

What we can hear is ~20 Hz – 20kHz and sonograms are 2-20 MHz

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# Material interaction with sound

What kind of interactions exist between sound and matter?

- Reflection
- Transmission
- Absorption
- Refraction
- Diffraction
- Scattering

For the purposes of ultrasound, we will largely focus on reflections though not exclusively.

# Material interaction with sound

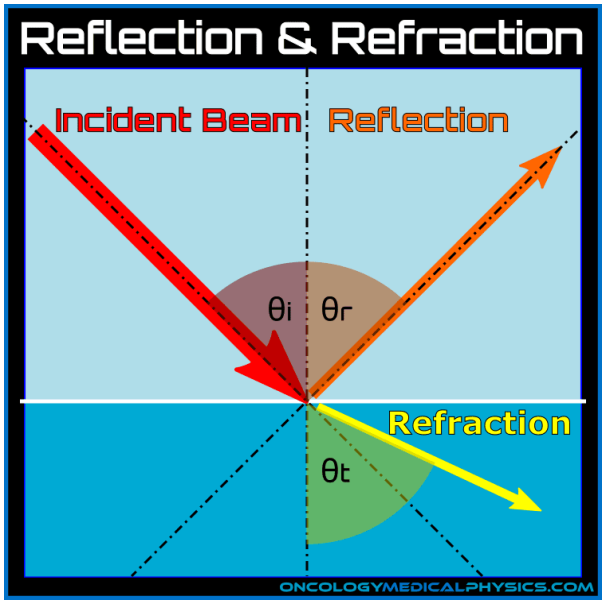
**In optics:**

$$\theta_i = \theta_r$$
$$n_i \sin\theta_i = n_t \sin\theta_t$$

**In acoustics:**

$$\theta_i = \theta_r$$
$$\frac{\sin\theta_i}{v_i} = \frac{\sin\theta_t}{v_t}$$
$$Z = \rho v$$
$$\frac{\rho_i \sin\theta_i}{Z_i} = \frac{\rho_t \sin\theta_t}{Z_t}$$

$$\frac{I_r}{I_i} = \left(\frac{Z_t - Z_i}{Z_t + Z_i}\right)^2$$




- Acoustic reflection is based on the difference of acoustic impedances
- Most of the contrast you see on ultrasound is based on this

# Acoustic properties of biological tissues

| Tissue | Density ($Kg/m^3$) | Longitudinal Wave Velocity (m/s) | Acoustic Impedance ($Kg/m^2s$) $\times 10^6$ |
|---|---|---|---|
| Air | 1.2 | 330 | 0.0004 |
| Lung | 400 | 440–500 | 0.18–0.20 |
| Adipose tissue | 920 | 1460 | 1.35 |
| Water | 1000 | 1480 | 1.48 |
| Liver | 1060 | 1550 | 1.64 |
| Spleen | 1060 | 1560 | 1.65 |
| Blood | 1060 | 1560 | 1.62 |
| Kidney | 1040 | 1560 | 1.62 |
| Muscles | 1070 | 1590 | 1.70 |
| Connective tissue | 1120 | 1610 | 1.80 |
| Cartilage | 1100 | 1665 | 1.85 |
| Skin | 1150 | 1730 | 1.99 |
| Bone | 1380–1810 | 2700–4100 | 3.75–7.38 |

$$Z = \rho v$$

Quarato, Carla & Lacedonia, Donato & Salvemini, Michela & Tuccari, Giulia & Mastrodonato, Grazia & Villani, Rosanna & Fiore, Lucia & Scioscia, Giulia & Mirijello, Antonio & Saponara, Annarita. (2023). A Review on Biological Effects of Ultrasounds: Key Messages for Clinicians. Diagnostics. 13. 855. 10.3390/diagnostics13050855.

# Material interaction with sound: attenuation

As a sound wave penetrates into the material, it decreases in intensity. But how?

Empirically:

$$P(x + \Delta x) = P(x)e^{-\alpha \Delta x}$$

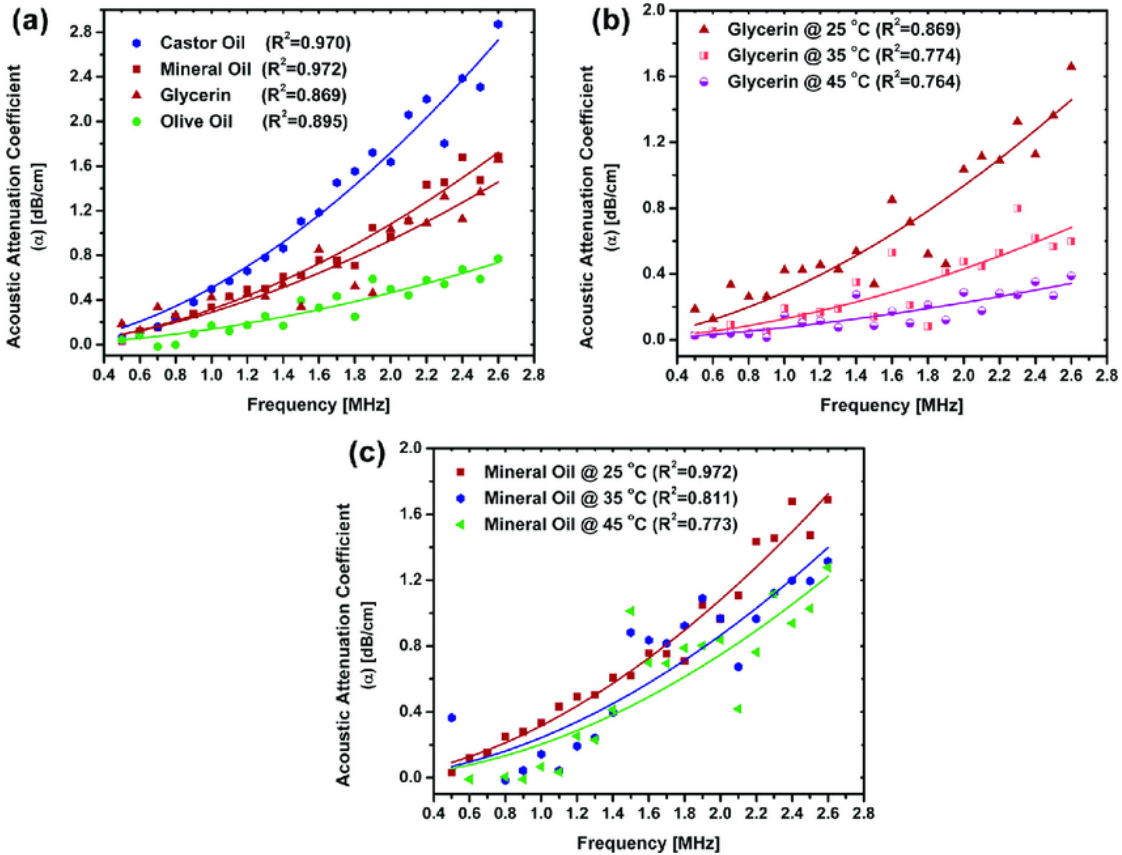
$\alpha$ is an attenuation coefficient with units 1/m

$\alpha = \alpha_a + \alpha_s$ Attenuation generally comes from absorption and scattering

$\alpha = \alpha_0 f^{\gamma}$ Just like optical refractive index was strongly wavelength dependent, the acoustic absorption coefficient is frequency dependent.

$\gamma$ is generally between 0 and 4
For soft materials, often $1 < \gamma < 2$
For metals, crystals it's around 1
For liquids $\gamma \sim 2$

# What does this acoustic attenuation depend on?




Generally, absorption is higher at higher frequencies

Then why not use super low frequency / long wavelength)?

Long wavelength = lower resolution

- Similar balance as with optics. Near infrared given better penetration but worse resolution

Thanh, Pham Van et al. "Effect of Temperature on Ultrasonic Velocities, Attenuations, Reflection and Transmission Coefficients between Motor Oil and Carbon Steel Estimated by Pulse-echo Technique of Ultrasonic Testing Method." (2015).

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# Instruments in acoustics

1. Source of signal
   - Light, sound, radioactive decay, magnetic moment etc.

2. Method of detection
   - How does the signal get captured?
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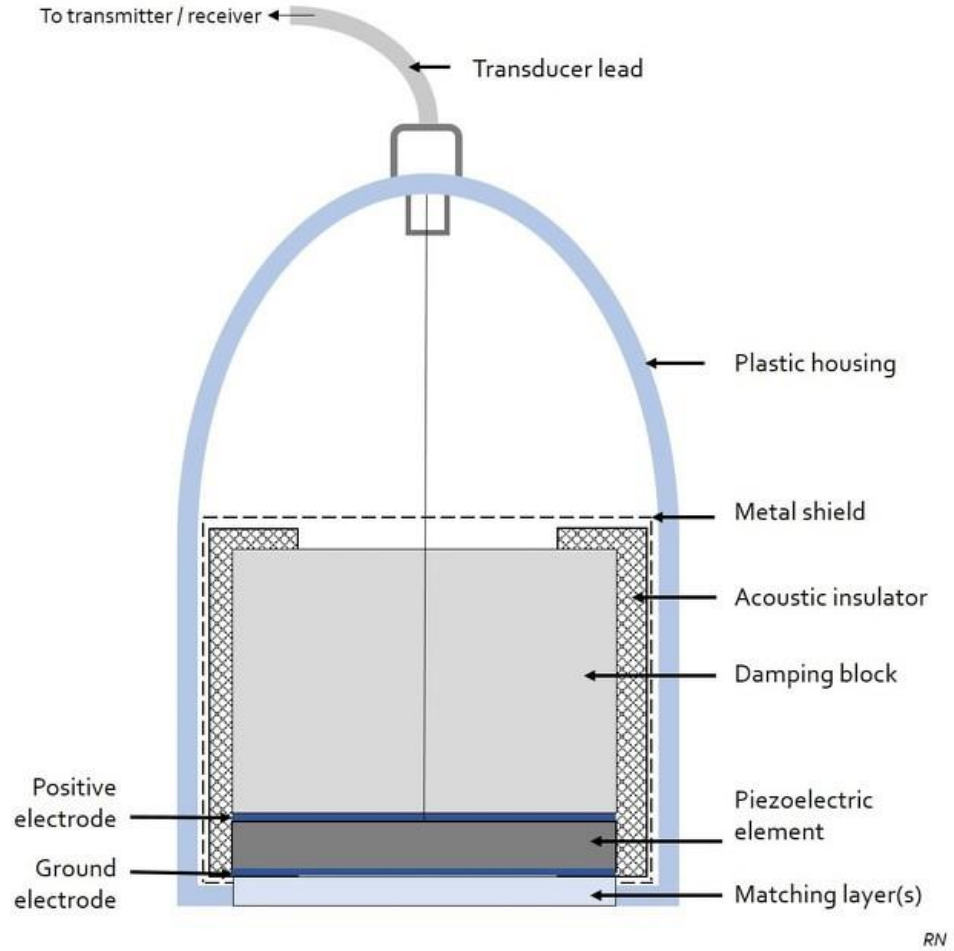
# Instruments in acoustics



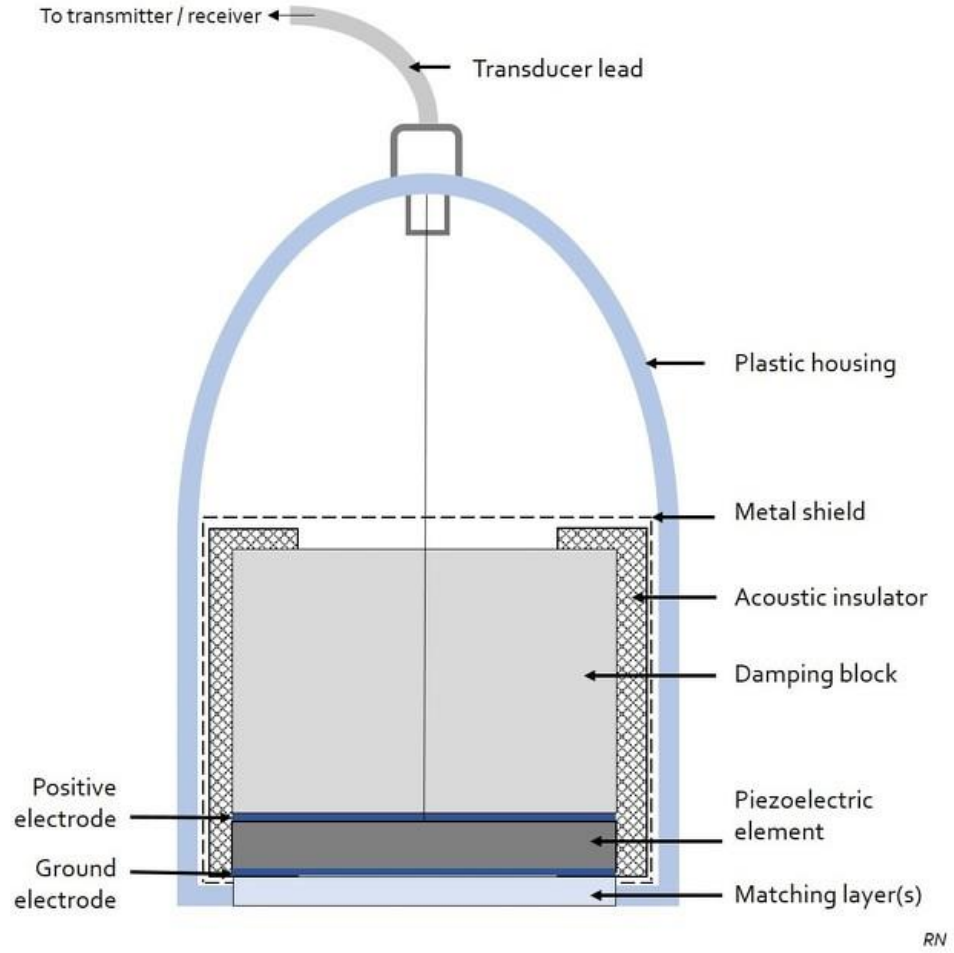

**Acoustic transducer:**

**Matching layer(s):**
Materials that have a Z in between the piezoelectric element (that produces the sound waves) and patient skin.

**Piezo element:**
A crystal (usually) that deform in response to an electric field. This deformation is used to create a sound wave for imaging.

Similarly, a reflected wave will deform the crystal and generate an electric signal to be translated into readable data.

# Instruments in acoustics



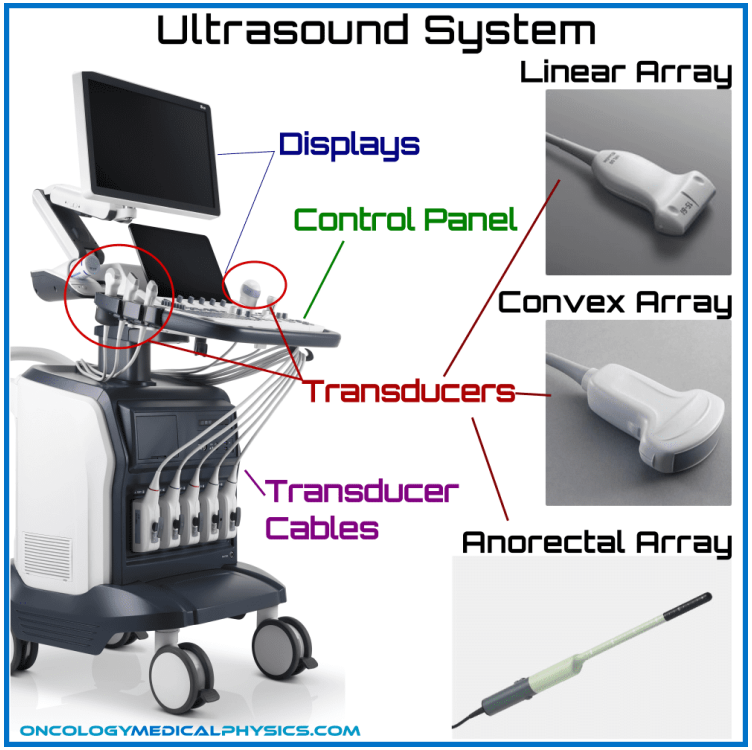

**Transmitter receiver**
Sends and receives electric signals

**Damping block**
When a sound wave comes back from a tissue, it continues past the piezoelectric element. Since it can create artifacts it's best to get rid of it, which is the function of the damping block.

**Acoustic insulator**
Insulates from extraneous signals not coming from piezo or the patient tissue.

**Metal shield**
Insulates from electrical noise

# Instruments in acoustics



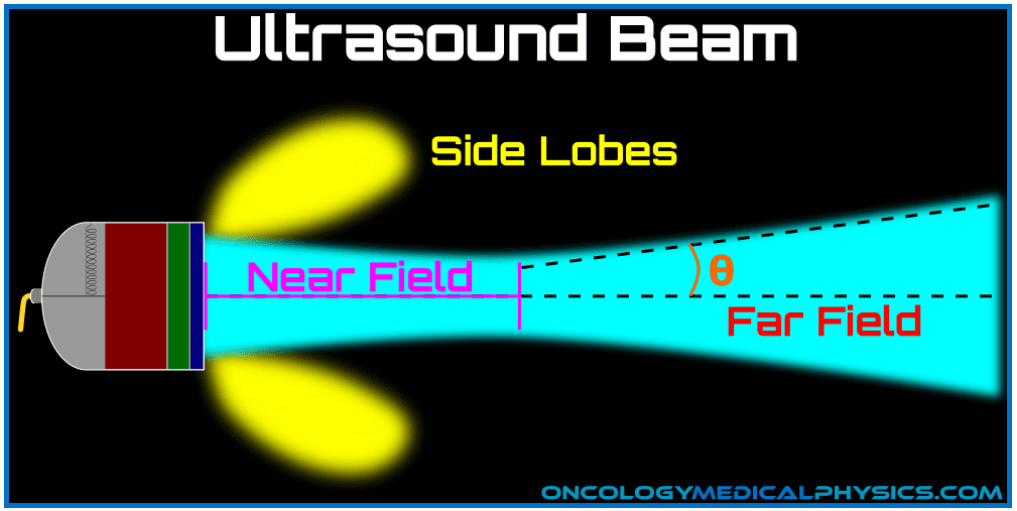

**Linear arrays** usually use higher frequencies with better spatial resolution but worse penetration.

**Convex arrays** usually use lower frequencies and can penetrate deeper.

**Anorectal arrays** basically what they sound like. They can have radial array for a 360 view and often use higher frequency for better resolution

Arrays usually have 128 to 512 elements to image

# Sound beam profile




r is the radius of the transducer

**Near field ~** $\frac{r^2}{\lambda}$

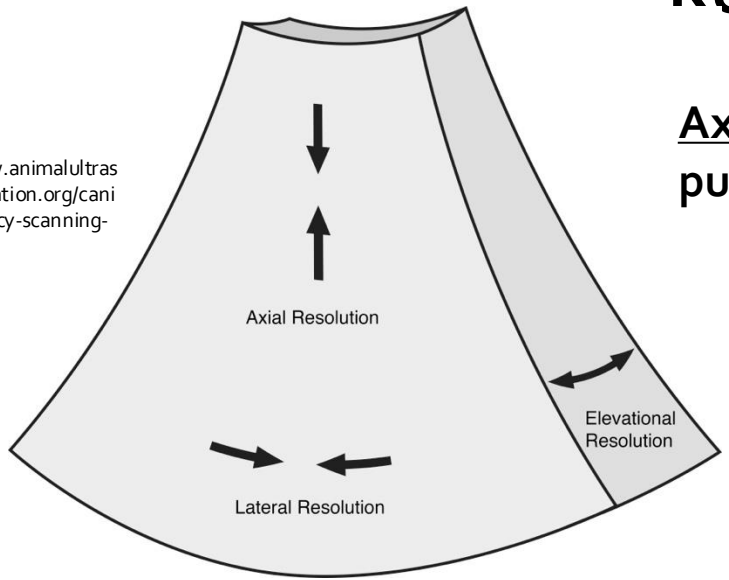
**Far field divergence**

$$\sin(\theta) \sim \frac{2\,\lambda}{r}$$

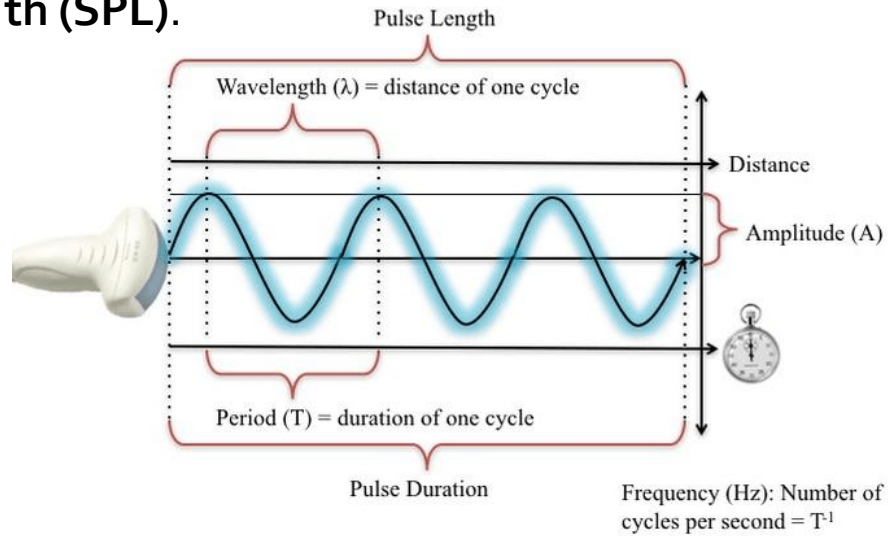
The side lobes are also products of interference patters and are largely a nuisance in acoustic imaging

# Resolution

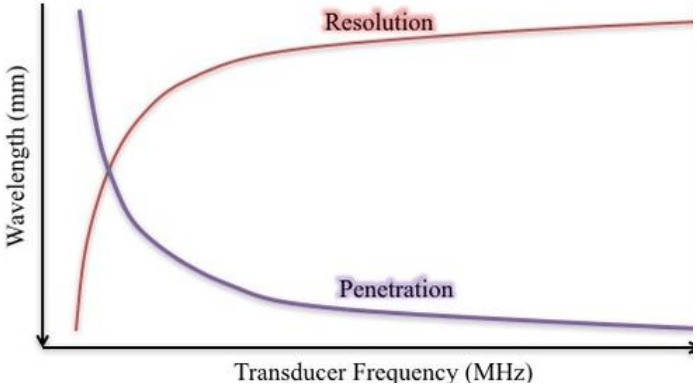
https://www.animalultrasoundassociation.org/canine-pregnancy-scanning-module-4/




**<u>Axial resolution</u>** is largely determined by the **spatial pulse length (SPL)**.



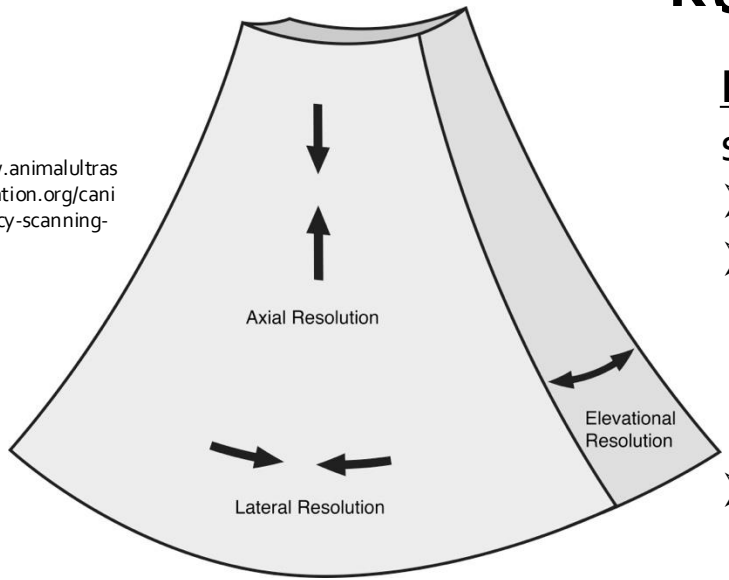

https://www.impocus.ca/acoustic-basics---understanding-the-b




- Duration of the pulse
- Frequency / wavelength of sound employed
- Resolution sometimes defined as ½ of SPL
- "Ringdown" can also affect the resolution

# Resolution

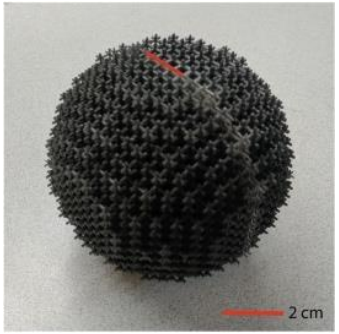
https://www.animalultrasoundassociation.org/canine-pregnancy-scanning-module-4/

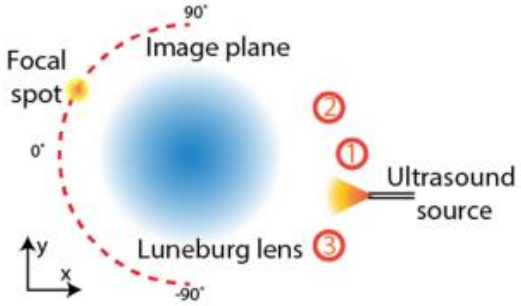



**<u>Lateral resolution</u>** depends on how well focused the sound beam is.

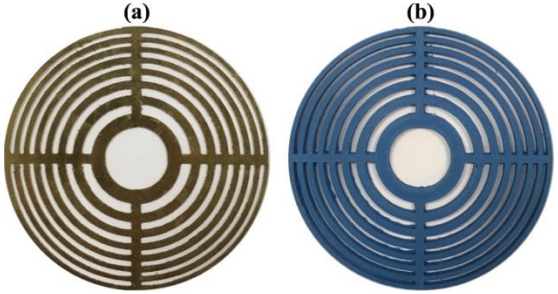
- How many piezo elements are fired
- Divergence of the beam
  - Higher frequency has less divergence
  - Higher frequency limits penetration depth

- Can use acoustic lenses to focus the beam



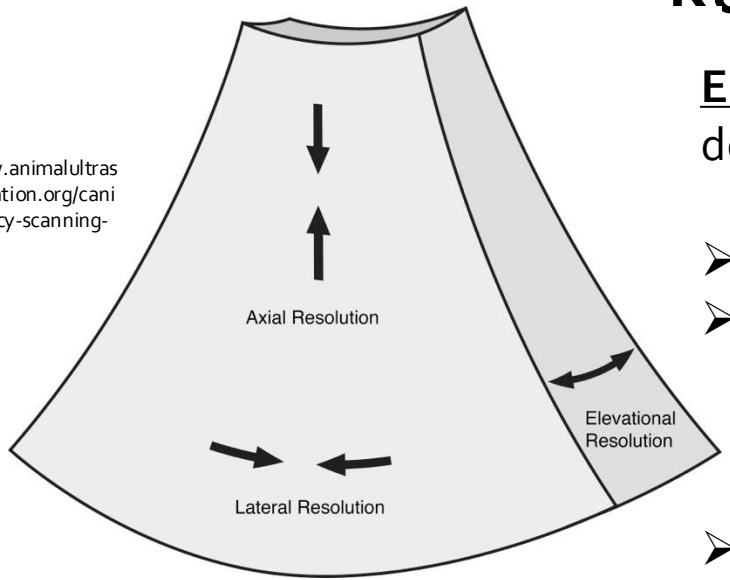

Xie, Y., Fu, Y., Jia, Z. *et al.* Acoustic Imaging with Metamaterial Luneburg Lenses. *Sci Rep* **8**, 16188 (2018). https://doi.org/10.1038/s41598-018-34581-7




Tarrazó-Serrano, D., Pérez-López, S., Candelas, P. *et al.* Acoustic Focusing Enhancement In Fresnel Zone Plate Lenses. *Sci Rep* **9**, 7067 (2019). https://doi.org/10.1038/s41598-019-43495-x

# Resolution

https://www.animalultrasoundassociation.org/canine-pregnancy-scanning-module-4/




**<u>Elevational resolution</u>**, similar to lateral resolution depends on how well the beam is focused.

- The height of the piezo elements
- Divergence of the beam
  - Higher frequency has less divergence
  - Higher frequency limits penetration depth
- Can use acoustic lenses to focus the beam
- This resolution gives the "slice thickness"

# Ultrasound brief history

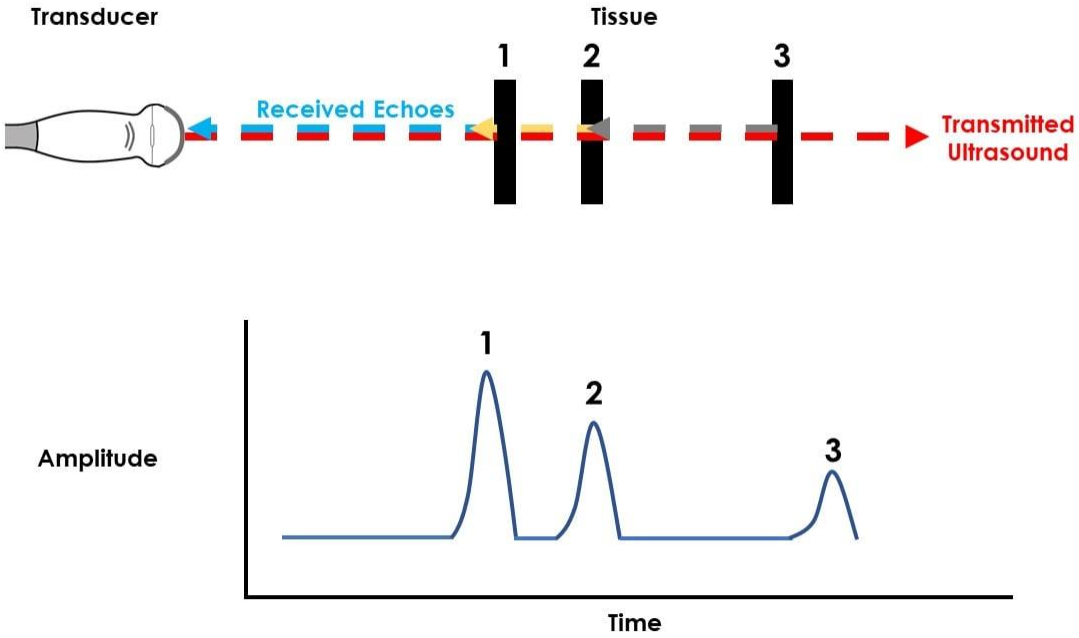
- First use of ultrasound for detection was during WWI and WWII to detect submarines etc
- 1940's is the first recorded attempt to use sound to detect brain tumors
- 1948 first reported successful clinical application by George Ludwig for gallstones etc
- 1958 first use of ultrasound in pregnancy by Ian Donald. Together with engineer Tom Brown, the first sonogram machine is made
- Similar time frame another clinician / engineer pair, John Reid and John Wild, use sonograms to detect tumors in breast cancer
- 1970's live image sonograms

The prototype scanner that Donald and Brown built in 1957


Wild and Reid's setup reported in Electronics in 1955

# Generating acoustic images: A-mode imaging

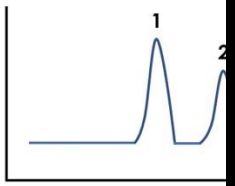
**A-mode:** "Amplitude mode." Not used so much today because of limited information

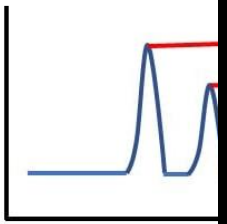


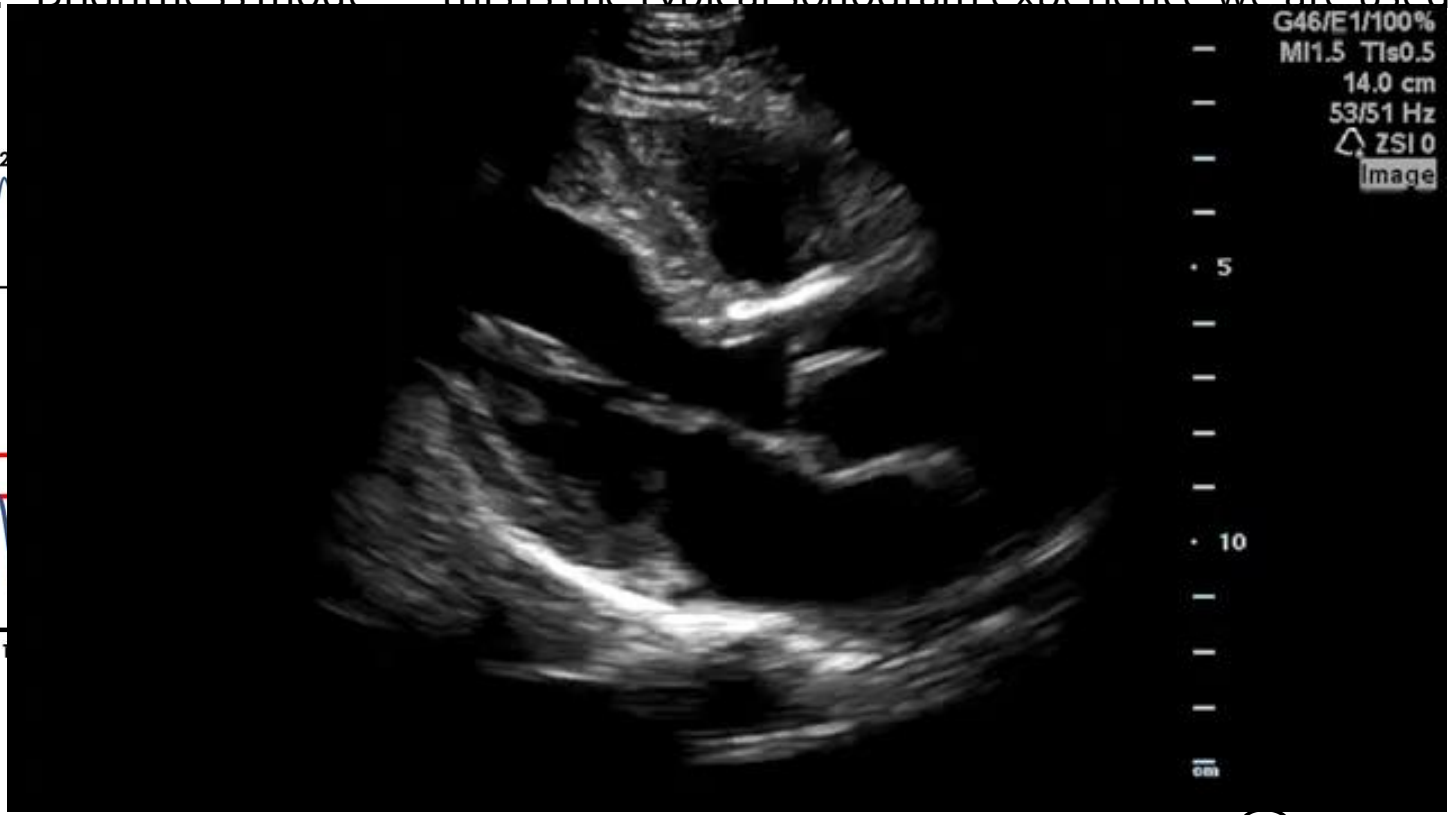

https://www.imv-imaging.com/us/2023/04/news-the-a-b-ms-ultrasound-modes-explained/

# Generating acoustic images: B-mode imaging

**B-mode:** "Brightness mode" -- this is the typical sonogram experience we are used to



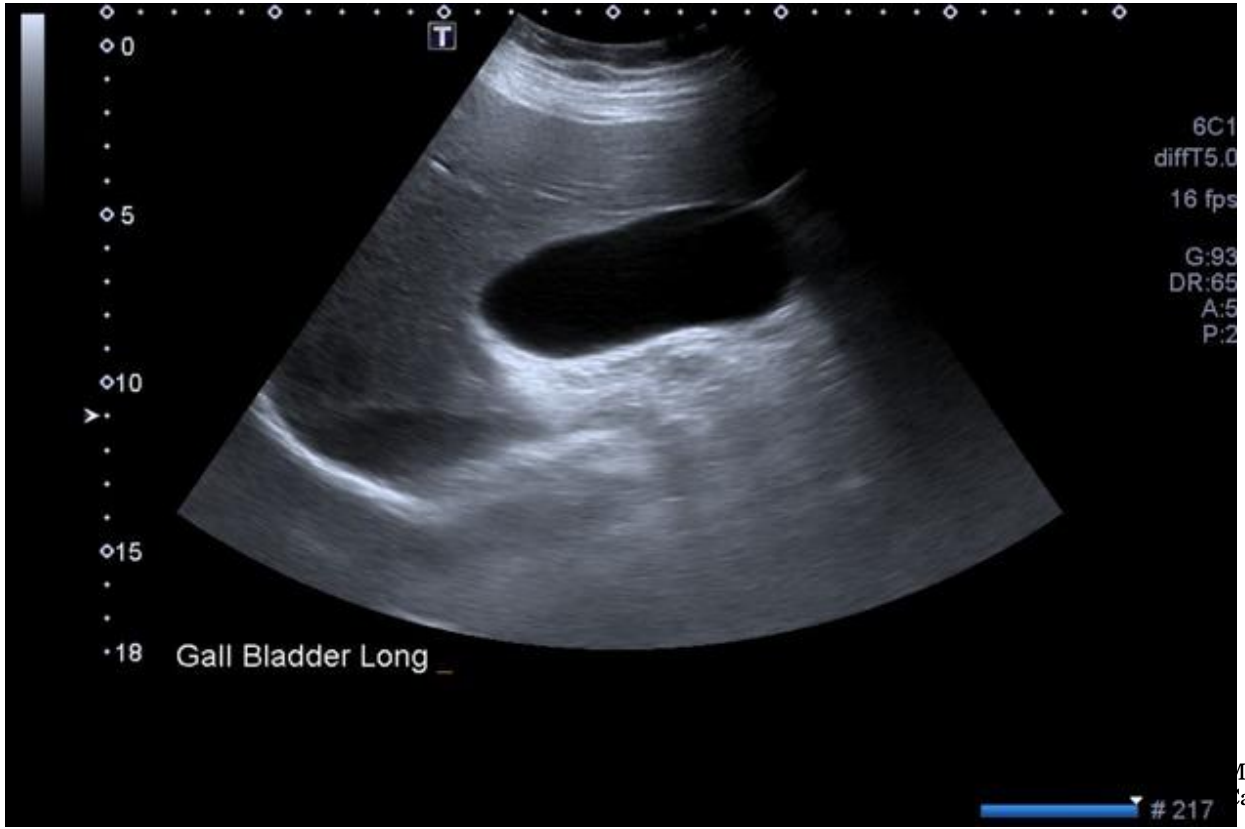



A-mode

B-mode

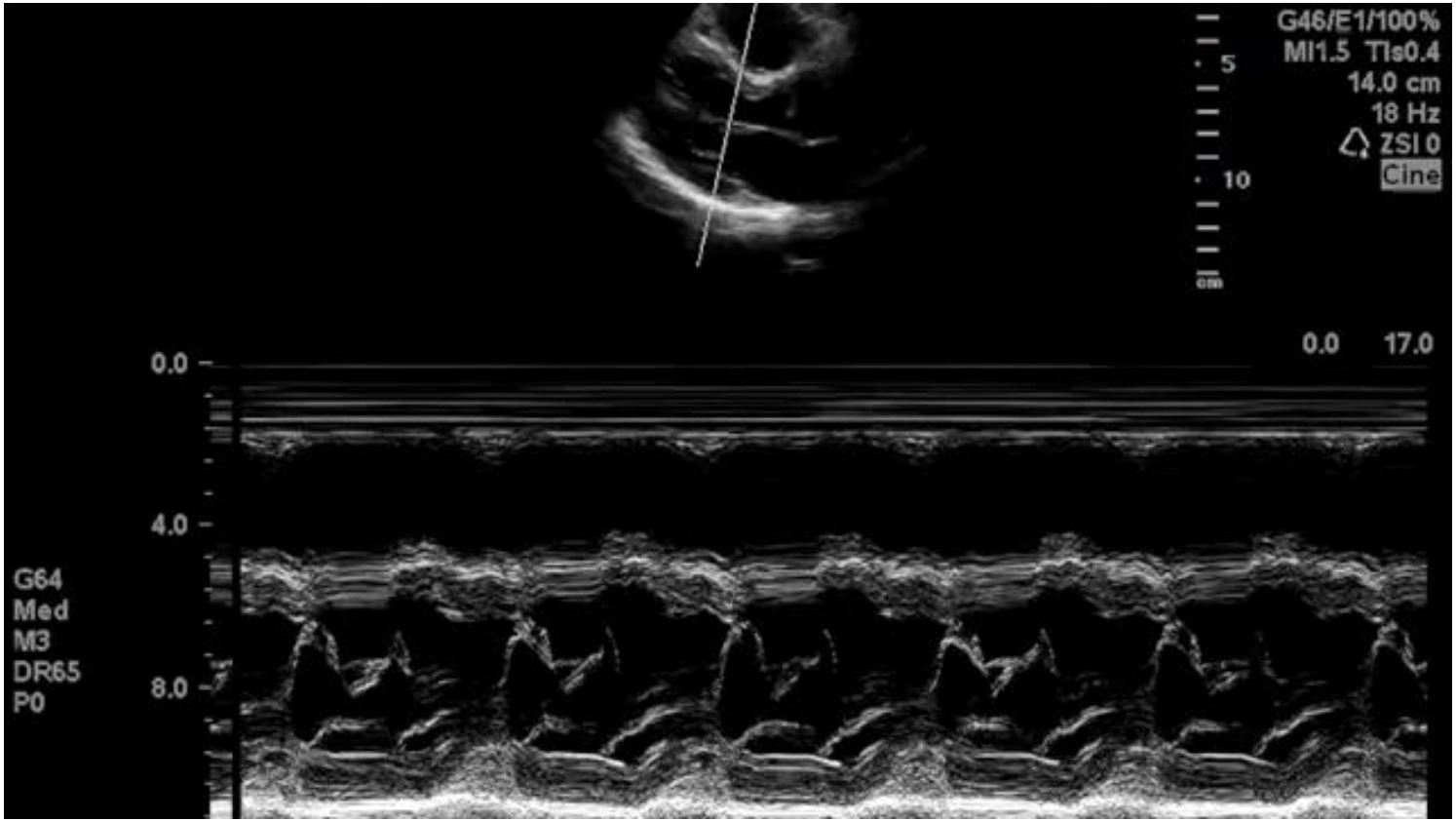
# Generating acoustic images: C-mode imaging

**C-mode:** "Constant depth mode."



# Generating acoustic images: M-mode imaging

**M-mode:**"Motion mode."



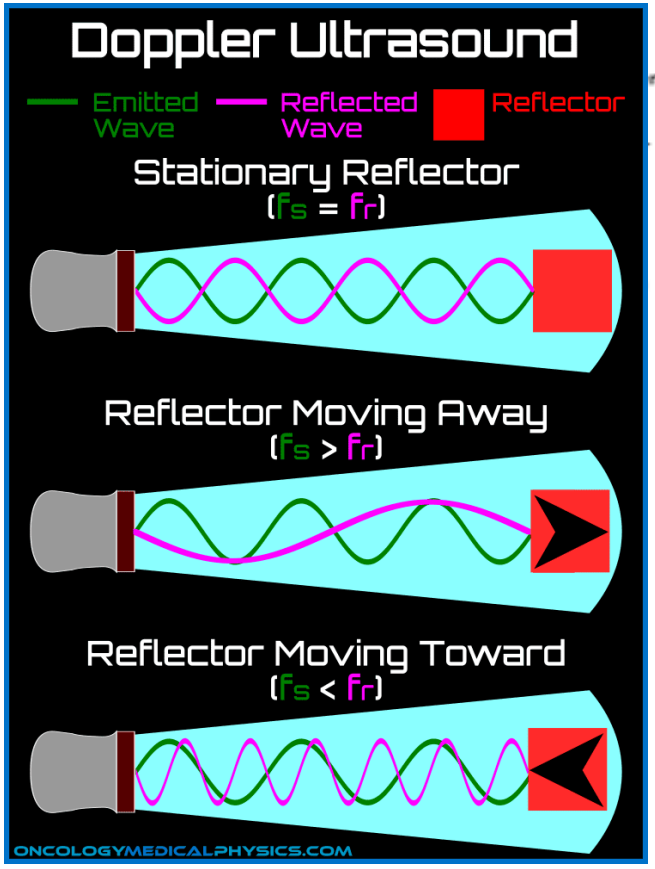

Kettering

# Doppler effect

**Doppler effect:** The perceived frequency changes when either the source of signal or the observer (or both are moving).

$$f_o = \left(\frac{v \pm v_o}{v \mp v_s}\right) f_s$$

Top sign is when the source and the observer are moving closer to together




- In Doppler sonogram, the moving source is often blood. Blood is the reflector
  - Assess health of arteries
  - Identify aneurisms
  - Blood flow from the heart
  - Baby blood flow in uterus

# Elastography

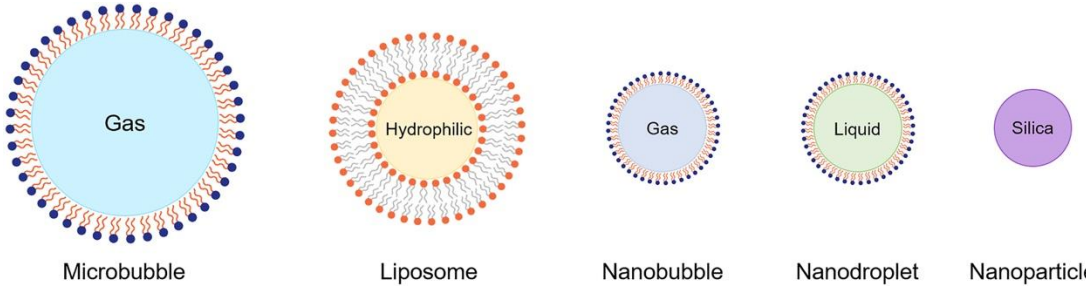
**Elastography** Mapping out the elasticity of tissues with ultrasound

- Can deform with sound waves and externally image the deformation $\Delta P = -\varepsilon \, \mathrm{B}$
- Can measure speed of sound in tissue and deduce change in stiffness $v = \sqrt{\frac{B}{\rho}}$
- Used in cancer as tumors are often stiffer (as in breast cancer)

# Acoustic contrast agents

Most contrast agents in sonograms involve some kind microbubbles or microparticles.

There are a few mechanisms of action that we can briefly explore




Zullino S, Argenziano M, Stura I, Guiot C, Cavalli R. From Micro- to Nano-Multifunctional Theranostic Platform: Effective Ultrasound Imaging Is Not Just a Matter of Scale. *Molecular Imaging*. 2018;17.

**Microbubbles**: stabilized bubbles introduced into the bloodstream. Bubbles are really flexible and give strong signal to visualize blood flow, blood vessels etc.

**Nanodroplets and nanoparticles**: contents can vaporize (or otherwise respond) with high ultrasound creating contrast only in places where the sound waves are sent. A common application is targeted imaging and delivery therapeutics of cancerous tissues.

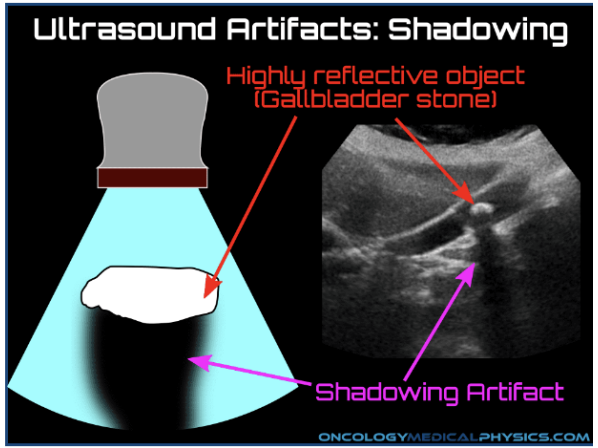
**Functionalized microbubbles or droplets**: Can functionalize the surface of bubbles or droplets to target specific sites.

# Types of artifacts to look out for

## Shadowing

**Appearance:** A region of hypo-intense signal often distal to high attenuation objects, such as bone.

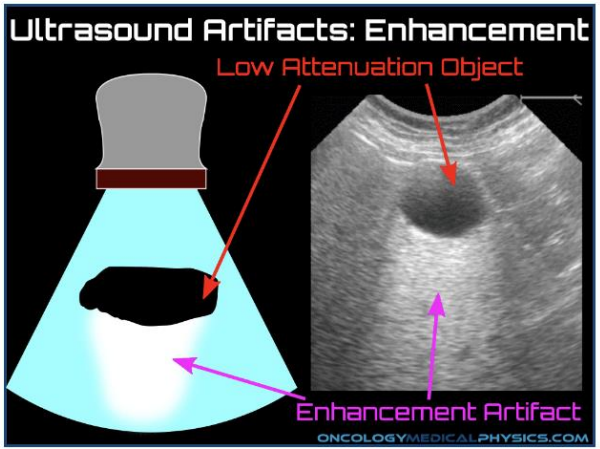
**Cause:** Attenuation by objects superficial to the artifact.




## Enhancement

**Appearance:** A region of hyper-intense signal often distal to low attenuation objects, such as uniform fluid-filled cavities.

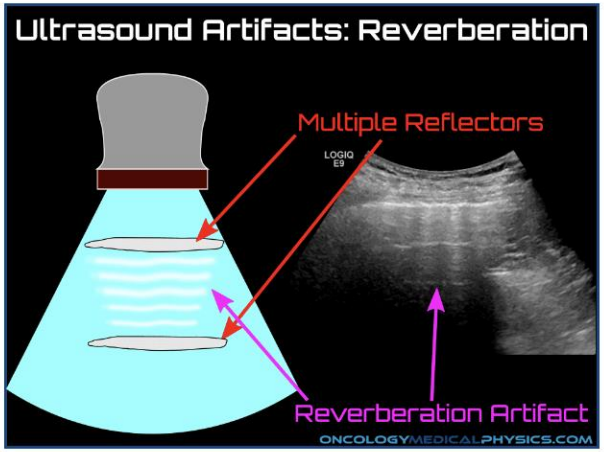
**Cause:** Lack of attenuation by objects superficial to the artifact.




## Reverberation

**Appearance:** Hyper-intense repeating signal.

**Cause:** Repeated reflections between two closely spaced objects.

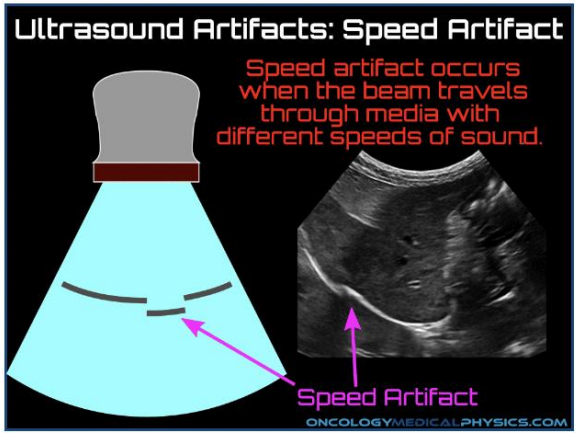


# Types of artifacts to look out for

## Speed Artifact

**Appearance:** Abrupt mis-mapping of an object along the direction of the beam axis.

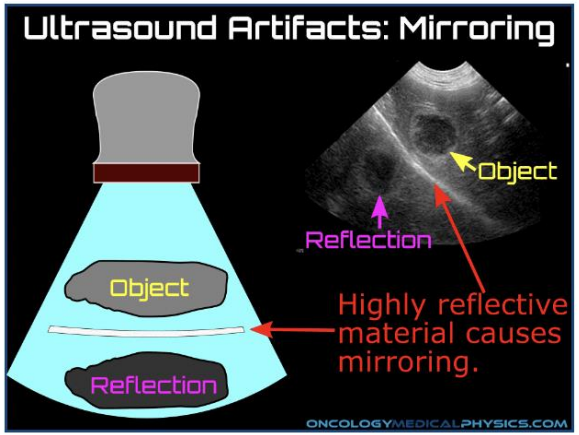
**Cause:** Variations of the speed of sound between beam projections.




## Mirroring

**Appearance:** A second inverted object appears beyond a highly reflective surface.

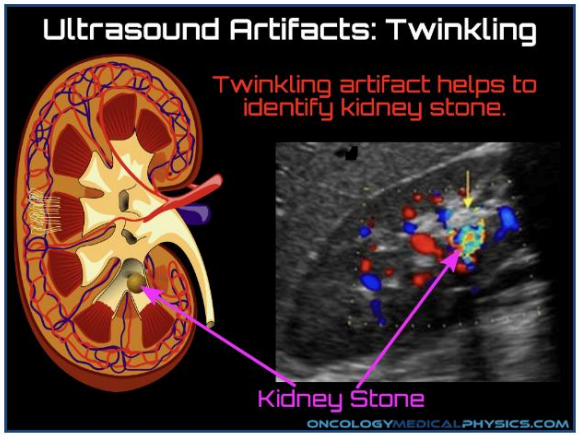
**Cause:** Multiple beam reflections between the object and the highly reflective surface.




## Twinkling Artifact

**Appearance:** In color Doppler imaging mode, a region appears as a rapidly changing mix of colors.

**Cause:** The presence of small strongly reflective objects within the Doppler study.




**Energy from side lobes and unexpected refractions can also cause artifacts**

# Applications in cancer

**Detection of tumors**: Tumors are often distinguishable from healthy tissues with acoustics due to their reflective properties

**Elastography** : Tumor elastic properties may also be used to distinguish from benign tissues.

**Targeted treatment**: Using nanodrops and other nanoparticles where the contents are activated with ultrasound can be useful in treating specific malignant targets

**Combination of modalities**: Ultrasound can be used in combination with other imaging (like optics) and clinical (like acoustic-guided surgery) approaches.

# Optoacoustics or photoacoustics

Light is used to stimulate a tissue and cause a vibration that is detected by sonogram

- Light is absorbed by tissues (remember light absorption is wavelength dependent and differs for different tissues).
- The absorption causes heating, which in turn causes expansion. The expansion creates a vibration detectable on an acoustic transducer.
  - Interesting that the stimulation is from within
- Allows for more precise stimulation region
- Even though the detection is with acoustics, the received information can be interpreted as a light absorption measurement.

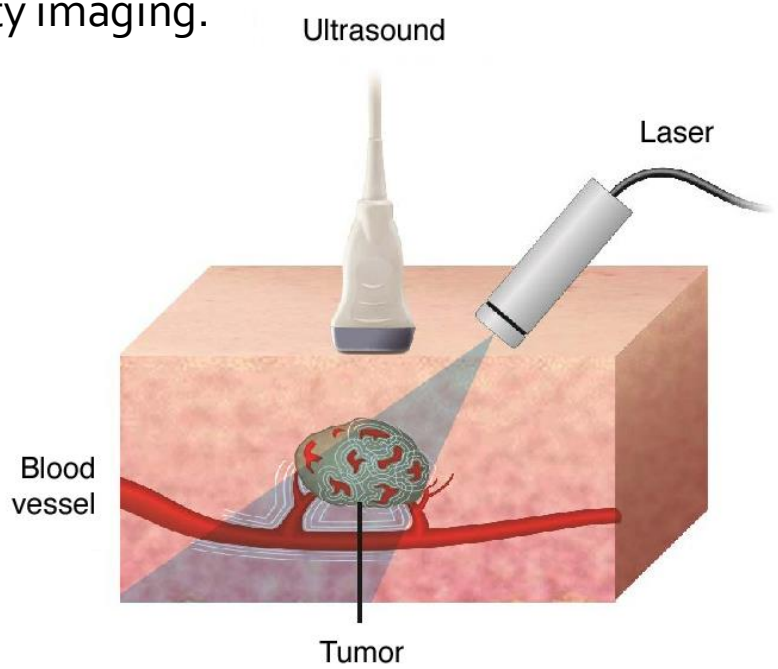

- Oxygenation in blood is one of the most common phenomena that causes differential light absorption and is thus measured in photoacoustics.

# Photoacoustics cnt'd

- Light absorption results from either oxygenation or tissue composition opens the possibility of either functional or material property imaging.

- Melatonin too has pretty distinct absorption properties making it a target of photoacoustics in skin cancer.

- Enhanced vasculature often associated with cancer can also stand out in photoacoustics due to the presence of hemoglobin




Valluru, Keerthi S and Juergen K Willmann. "Clinical photoacoustic imaging of cancer." *Ultrasonography* 35 (2016): 267 - 280.

# 5 minute feedback

https://forms.gle/NGWk7X9T3Sjaoviq5

# Absorption coefficients in biomaterials

| Tissue/Medium | Attenuation Coefficient (dB/cm/MHz) | Acoustic Impedance (Mrayl) |
|---|---|---|
| Water | 0.0022 | 1.5 |
| Blood | 0.15 | 1.6 |
| Soft tissue | 0.75 | 1.6 |
| Air | 7.50 | 0.00001 |
| Bone | 15.0 | 8.0 |
| Fat | 0.63 | 1.4 |
| Kidney | 1.0 | 1.6 |
| Lens of eye | 0.05 | 1.7 |

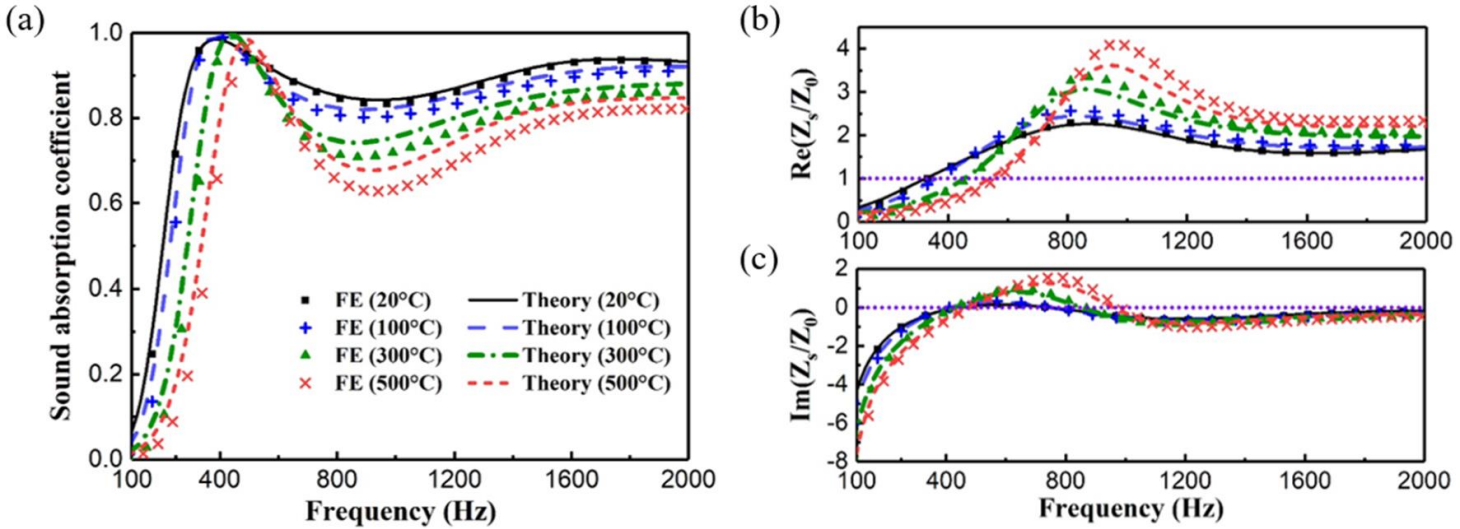
Shankar, Hariharan & Pagel, Paul. (2011). Potential Adverse Ultrasound-related Biological Effects A Critical Review. Anesthesiology. 115. 1109-24. 10.1097/ALN.0b013e31822fd1f1.

# What do Z and $\alpha$ depend on?

$$Z = \rho v \quad \left.\begin{array}{l} \\ v = \sqrt{\dfrac{B}{\rho}} \end{array}\right] \quad Z = \sqrt{\rho B}$$

How do you expect Z to change with:

(a) Frequency of sound
(b) Temperature




Liu, Q., Liu, X., Zhang, C. *et al.* High-Temperature and Low-Frequency Acoustic Energy Absorption by a Novel Porous Metamaterial Structure. *Acta Mech. Solida Sin.* **34,** 872–883 (2021)

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